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10/588,597	02/04/2007	Akio Matsuhisa	5426FP-1	9532

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EXAMINER	
BAUGHMAN, MOLLY E	
ART UNIT	**PAPER NUMBER**
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/588,597	MATSUHISA ET AL.	
	Examiner	Art Unit	
	Molly E. Baughman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3 and 5-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3 and 5-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 August 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/7/06; 2/4/07; 11/2/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Information Disclosure Statement

1. The information disclosure statement (IDS) submitted on 8/7/2006 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. However, some citations have been either modified, or lined through for the following reasons:

a. Citation Nos.1-2, and 7 under Foreign Patent Documents, have been considered only for the submitted English *abstract*, as the remainder of the document is in a foreign language.

b. Citation Nos. 3-5 under Foreign Patent Documents, are not being considered as they are in a foreign language.

c. Citation Nos.1-2 under Non-Patent Literature Documents, are not being considered as they are in a foreign language.

2. The information disclosure statement (IDS) submitted on 2/4/07 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. However, some citations have been either modified, or lined through for the following reasons:

d. Citation No.1 under Foreign Patent Documents, is not being considered as it is in a foreign language.

e. Citation No.2-3 under Foreign Patent Documents, have been considered only for the submitted English *abstract*, as the remainder of the documents are in a foreign language.

3. The information disclosure statement (IDS) submitted on 11/2/07 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. However, some citations have been either modified, or lined through for the following reasons:

f. Citation No.1 under Non-Patent Literature Documents, corresponding to a Search and Examination Report, has been fully considered, although, it has been lined through since it is not an appropriate document for printed patents.

Claim Rejections - 35 USC § 112

4. Claims 1, 3, and 5-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

g. Claim 1 is confusing because it cannot be determined what is encompassed by "exposing." While claim 3 provides examples of what the step entails, the scope of the term is unclear.

h. Claim 6 is indefinite because the claim language renders the claim confusing. While it appears the claim provides limitations of the determining step to comprise hybridization of probes to the amplified nucleic acids, the claim as

written, including present and past tense, is confusing in terms of what is involved in the hybridization of the probes.

i. Claim 7 is confusing because it is unclear what is encompassed by "the known gene fragments." Claim 6 appears to describe the probes being complementary to known gene fragments, where the gene fragments are hypothetical and only exist if they are present when the probes hybridize to them in the amplified nucleic acids. As such, it is unclear if the known gene fragments are the actual probes, or they encompass something different.

j. Claim 8 is indefinite because the claim language renders the claim confusing. While it appears the claim provides limitations of the determining step to comprise the use of probes and a DNA microarray for detecting the amplified nucleic acids, the claim as written, including present and past tense, is confusing in terms of what is involved in the use of the DNA microarray and probes.

k. Claims 11-18 are confusing because the claims rely on an intended use of the kit for the kit's contents and do not actually specify what is in the kit. Therefore, the contents and scope of the kit is unclear and indefinite. While claim 18 provides limitations for the contents of the kit, it depends from a claim which is indefinite.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 1, 3, 9-10 and 19 are rejected under 35 U.S.C. 102(e) as being anticipated by Chu et al. (US 6,703,247).

Regarding claim 1, Chu et al. teach a nucleic acid detection method comprising: fixing a cell-containing sample in divided compartments of a support; exposing nucleic acids contained in the sample; performing PCR by placing a PCR mixture, containing primers for amplifying a target nucleic acid, into the compartments of the support; determining whether amplified nucleic acids in a PCR solution contains contain the target nucleic acid (see Figures 1B, 1E, 2A+B, 7E; col.2, lines 34-40; col.21-22, Example 3; and col.24-25, Example 4).

Regarding claim 3, Chu teaches the method, wherein the nucleic acid exposing step is performed by one or more methods selected from the group consisting of a detergent treatment method, an enzyme treatment method, and a heat treatment method (col.24, lines 28-35).

Regarding claims 9-10, Chu teaches the method wherein the sample originates in biological sources, and wherein the biological sample originates from humans (col.18, lines 42-45).

Regarding claim 19, Chu teaches the method wherein the support with the divided compartments is shaped to fit a gene amplifier for PCR (thermal cycler) (col.16, lines 50-51; col.24, lines 59-62).

7. Claims 1, 3, 9-17 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Cloyd et al. (US 6,448,014).

Regarding claim 1, Cloyd et al. teach a nucleic acid detection method comprising: fixing a cell-containing sample in divided compartments of a support; exposing nucleic acids contained in the sample; performing PCR by placing a PCR mixture, containing primers for amplifying a target nucleic acid, into the compartments of the support; determining whether amplified nucleic acids in a PCR solution contains contain the target nucleic acid (see Example 2, col.5).

Regarding claim 3, Cloyd teaches the method, wherein the nucleic acid exposing step is performed by one or more methods selected from the group consisting of a detergent treatment method, an enzyme treatment method, and a heat treatment method (col.5, lines 21-26).

Regarding claims 9-10, Cloyd teaches the method wherein the sample originates in biological sources, and wherein the biological sample originates from humans (col.5, line 2).

Regarding claim 19, Cloyd teaches the method wherein the support with the divided compartments is shaped to fit a gene amplifier for PCR (thermal cycler) (col.5, lines 30-32).

Regarding claims 11-17, Cloyd teaches a kit for practicing the method of the invention (col.4, lines 44-64). It is noted that although Cloyd does not teach the kit according to specific intended uses specified in claims 14-17, this is an intended use of the kit and as explained above, the claims are indefinite since they do not specify the contents of the kit.

8. Claims 1, 3, 5-6, 9-10 and 19-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Blumenfield et al. (US 6,228,634 B1).

Regarding claim 1, Blumenfield et al. teach a nucleic acid detection method comprising: fixing a cell-containing sample in divided compartments of a support; exposing nucleic acids contained in the sample; performing PCR by placing a PCR mixture, containing primers for amplifying a target nucleic acid, into the compartments of the support; determining whether amplified nucleic acids in a PCR solution contains contain the target nucleic acid (see Figure 1; col.3, lines 58-61; col.4, lines 1-14, 64-67; col.8, lines 9-28; col.13, lines 54-57, 66-67).

Regarding claim 3, Blumenfield teaches the method, wherein the nucleic acid exposing step is performed by one or more methods selected from the group consisting of a detergent treatment method, an enzyme treatment method, and a heat treatment method (col.21, lines 1-3).

Regarding claim 5, Blumenfield teaches the method, wherein the amplified nucleic acids are labeled in step of performing PCR (col.11, lines 18-21; col.13, lines 15-31; col.18, lines 9-15).

Regarding claim 6, Blumenfield teaches the method as set forth in claim 5, wherein, in the determining step, a target nucleic acid is detected if there is complementary hybridization of known gene fragments with probes, for which the nucleic acids amplified and labeled in the nucleic acid amplifying step of performing PCR are used (col.18, lines 36-47; col.22, lines 7-9).

Regarding claims 9-10, Blumenfield teaches the method wherein the sample originates in biological sources, and wherein the biological sample originates from humans (col.20, lines 51-53).

Regarding claim 19, Blumenfield teaches the method wherein the support with the divided compartments is shaped to fit a gene amplifier for PCR (thermal cycler) (col.7; col.10, lines 58-67).

Regarding claim 20, Blumenfield teaches the method wherein in the determining step, the target nucleic acid is detected by electrophoresis (col.11, lines 30-54, i.e. southern or northern analysis which involves electrophoresis).

9. Claims 11-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Krystosek et al. (US 5,264,343).

Krystosek teaches a kit useful for practicing the method of the invention according to claims 1 and 10 (col.10, lines 34-58 and claims 13-20). It is noted that although Krystosek does not teach the kit according to specific intended uses specified in claims 13-17, this is an intended use of the kit and as explained above, the claims are indefinite since they do not specify the contents of the kit.

10. Claims 11-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Saunders et al. (US 6,087,134).

Saunders teaches a kit useful for practicing the method of the invention according to claims 1 and 10 (col.12, lines 36-43). It is noted that although Saunders does not teach the kit according to specific intended uses specified in claims 13-17, this is an intended use of the kit and as explained above, the claims are indefinite since they do not specify the contents of the kit.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 7-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blumenfield et al. (US 6,228,634 B1), in view of Stapleton et al (US 6,103,192).

The teachings of the primary reference are discussed above. Although Blumenfield discusses hybridization of known gene fragments in the nucleic acid amplified via PCR to probes, he does not discuss the method where the probes are fixed on a support in advance [i.e. claim 7]. He also does not discuss the method wherein a target nucleic acid in the amplified nucleic acids from claim 5 is detected with the use of a DNA microarray and probes [i.e. claim 8].

Stapleton discusses a similar method wherein various biological specimens are collected, dried, transported, stored and processed on matrixes which adhere cells and viruses. The method involves fixing such samples to the matrixes, exposing the samples by heating them (col.17, lines 31-32), applying the matrixes to thin-walled tubes for amplification (col. 17, lines 23-35; col.22, Example 22), and detection by either gel electrophoresis (col.17, lines 10-15; col.22, Example 22), or by applying the amplified product and detector probes to a probe array comprising capture oligonucleotides (col.16, lines 9-60; col.24, lines 21-50 (Example 7)).

One of ordinary skill in the art would have been motivated to modify the method of Blumenfield et al. to use an immobilized probe detection system, particularly through the use of a DNA microarray and probes because it was conventional in the art at the time of the invention to detect amplified PCR products from in situ amplified specimens via the use of immobilized probes on a DNA microarray and detection probes, as demonstrated by Stapleton. Furthermore, Stapleton states that such a detection system

eliminates the need for gel elecrophoresis, less amplification product is needed as the sensitivity of the detection increases, and allows for multiple oligonucleotide sequences at different array positions to be analyzed in the same detection reaction (col.16, lines 26-28, 57-59). Since Blumenfield demonstrates the benefits of using probes to detect the amplified specimens and Stapleton demonstrate that it was not only conventional in the art at the time of the invention to use DNA microarrays (comprising immobilized probes) and detection probes for detecting PCR products from amplified specimens, but also provided greater detection efficiency and sensitivity for such detection, it would have been obvious to one skilled in the art to substitute one detection system for the other in order to achieve the predictable result of detecting amplified PCR products from in situ amplified specimens. Therefore, the skilled artisan would have had a reasonable expectation of success in using an immobilized probe detection system, particularly through the use of a DNA microarray and probes, in the method of Blumenfield et al. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods and use the detection system therein.

14. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Krystosek et al. (US 5,264,343), in view of Saunders et al. (US 6,087,134).

Regarding claims 11-18, Krystosek teaches a kit as set for in claim 11, which comprises: PCR reaction buffer, a mixture of deoxynucleoside triphosphate, labeled deoxynucleoside triphosphate; thermostable DNA polymerase; a sample-fixing support;

and an indicator for detecting amplified nucleic acids (col.10, lines 34-58 and claims 13-20).

Although Krystosek teaches the kit comprising amplification reagents, he is silent to whether the reagents include a target gene amplifying primer.

Saunders et al. teach a kit for analyzing fixed sample specimens via in situ PCR comprising slides, PCR primers, and PCR reagents (col.12, lines 36-43).

One of ordinary skill in the art would have been motivated to modify the kit of Krystosek et al. to include a target gene amplifying primer because not only was it conventional in the art at the time of the invention to package together reagents into a kit for the convenience of practicing methods, as demonstrated by both Krystosek and Saunders, but Saunders demonstrates that it was conventional in the art to include primers in such kits as a PCR reagent for use in methods involving in situ amplification. As such, the skilled artisan would have had a reasonable expectation of success in including a target gene amplifying primer in the kit of Krystosek et al. It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to make the claimed kit and include the claimed target gene amplifying primer therein.

Summary

15. No claims are free of the prior art.

16. Bagasra et al. (US 5,589,333), Bacallao et al. (US 7,186,507), and Koltai et al., "High Throughput Cellular Localization of Specific Plant mRNAs by Liquid-Phrase in

Situ Reverse Transcription-Polymerase Chain Reaction of Tissue Sections," Plant Physiology, Aug.2000, Voo.123, pp.1203-1212, are noted as references of interest.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Molly E. Baughman whose telephone number is 571-272-4434. The examiner can normally be reached on Monday-Friday 8-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Molly E Baughman
Examiner
Art Unit 1637

MEB 11/8/07

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
11/8/07